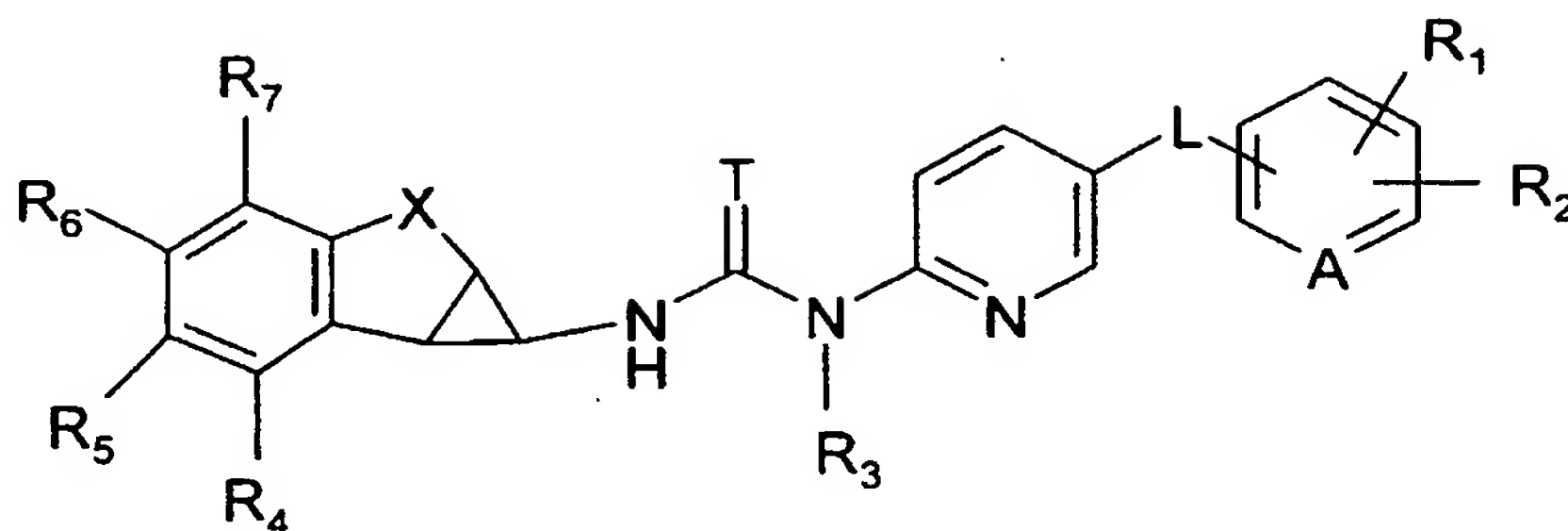


Claims

1. A compound of the formula Z:



where;

5 A is CH or N;

R₁ is a substituent to a carbon atom in the ring containing A selected from
-S(=O)_pRa,

where Ra is -C₁-C₄ alkyl, -OR_x, -NR_xR_x, -NHNHNR_xR_x, -
NHNHC(=O)OR_x, -NR_xOH;

10 -C(=O)-Rb,

where Rb is -C₁-C₄-alkyl, OR_x, -NR_xR_x, -NHNHNR_xR_x,
-NHC₁-C₃-alkyl-C(=O)OR_x

-NR_xRc,

where Rc is H, C₁-C₄ alkyl, -NR_xR_x; -C(=O)Rd, -CN, S(=O)_pR_x

15 where Rd is Rd is C₁-C₄-alkyl, -OR_x, -NR_xR_x
-C₁-C₃-alkyl-O-C₁-C₃alkylC(=O)OR_x,

-C₁-C₃-alkyl-COOR_x;

-C₁-C₃alkyl-OR_x

20 -(O-C₁-C₃alkyl)_q-O-R_x

a 5 or 6 membered aromatic ring have 1-3 hetero atoms;

p and q are independently selected from 1 or 2;

R_x is independently selected from H, C₁-C₄ alkyl or acetyl; or a pair of R_x can
together with the adjacent N atom form a pyrrolidine, piperidine, piperazine or

25 morpholine ring;

R_2 is a substituent to a carbon atom in the ring containing A and is H, halo, cyano, C_1 - C_4 -alkyl, halo C_1 - C_4 -alkyl;

L is $-O-$, $-S(=O)_r-$ or $-CH_2-$, where r is 0, 1 or 2;

R_3 is H, C_1 - C_3 alkyl;

5 R_4 - R_7 are independently selected from H, C_1 - C_6 alkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, halo C_1 - C_6 alkyl, C_1 - C_6 alkanoyl, halo C_1 - C_6 alkanoyl, C_1 - C_6 alkoxy, halo C_1 - C_6 alkoxy, C_1 - C_6 alkyloxy C_1 - C_6 alkyl, halo C_1 - C_6 alkyloxy C_1 - C_6 alkyl, hydroxy C_1 - C_6 alkyl, amino C_1 - C_6 alkyl, carboxy C_1 - C_6 alkyl, cyano C_1 - C_6 alkyl, amino, carboxy, carbamoyl, cyano, halo, hydroxy, keto;

10 X is $-(CR_8R_8')_n-D-(CR_8R_8')_m-$;

D is a bond, $-NR_9-$, $-O-$, $-S-$, $-S(=O)-$ or $-S(=O)_2-$;

n and m are independently 0, 1 or 2, provided that they are not both 0 when D is a bond;

R_8 and R_8' are independently H, C_1 - C_3 alkyl, halo C_1 - C_3 alkyl, hydroxy, or R_8 and R_8'

15 together with their adjacent C atom is $-C(=O)-$

R_9 is independently H, C_1 - C_3 alkyl;

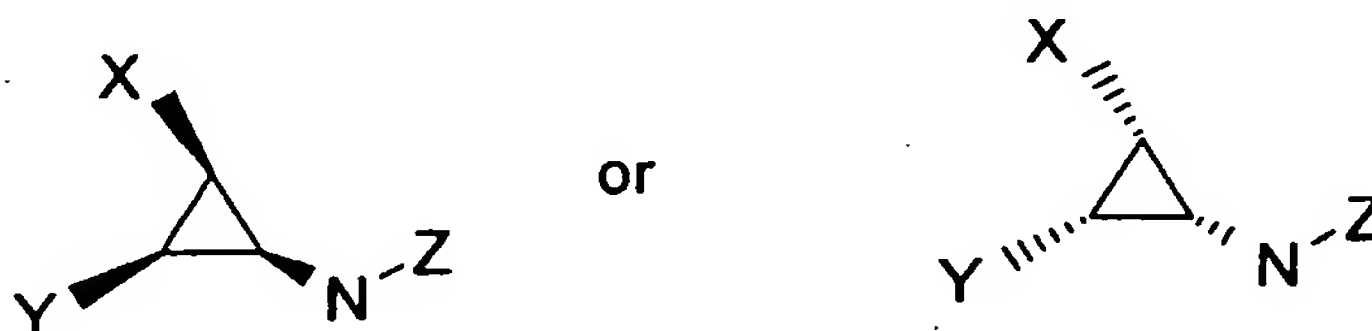
and pharmaceutically acceptable salts and prodrugs thereof;

with the proviso that R^2 as $-C(=O)R_b$ is not morpholinoketo-.

2. A compound according to claim 1, wherein T is O.

20 3. A compound according to claim 1, wherein R_3 is H.

4. A compound according to claim 1, wherein the cyclopropyl moiety has an enantiomeric excess of the conformation depicted in the partial formulae:



where X is as defined, Y is the bridge to the (substituted) phenyl ring depicted in formula I and Z is bond to the (thio)urea-pyridyl moiety depicted in formula Z.

25 5. A compound according to claim 1 wherein the compound of formula Z comprises an enantiomeric excess of the isomer showing negative optical activity.

6. A compound according to claim 1, wherein D is -O-
7. A compound according to claim 6, wherein n is 0 and m is 1.
8. A compound according to claim 1, wherein R₄ is hydrogen, fluoro or hydroxy.
- 5 9. A compound according to claim 1, wherein R₅ is hydrogen, fluoro, C₁₋₃ alkylcarbonyl or C₁₋₃alkyloxy.
- 10 10. A compound according to claim 1, wherein R₆ is hydrogen, halo, C₁₋₃alkyloxy, C₁₋₃alkylcarbonyl, cyano or ethynyl.
11. A compound according to claim 10, wherein R₆ is hydrogen, methoxy or fluoro.
12. A compound according to claim 1, wherein R₇ is hydrogen, cyano, halo, C₁₋₃alkyloxy, or C₁₋₃alkylcarbonyl.
- 15 13. A compound according to claim 12, wherein R₇ is cyano, fluoro or acetyl.
14. A compound according to claim 1, wherein R₅ and R₆ are H and R₄ and R₇ are fluoro.
- 20 15. A compound according to claim 1, wherein R₄ is fluoro, R₅ and R₆ are H, and R₇ is cyano or acetyl.
- 25 16. A compound according to claim 1, wherein L is -O-.
17. A compound according to claim 1, wherein R₁ is -S(=O)₂NR_xR_x, S(=O)₂C₁₋₄ alkyl, or S(=O)₂C₁₋₄ alkyl.
18. A compound according to claim 17, wherein R₁ is -S(=O)₂NH₂, -S(=O)₂NMe₂ or -S(=O)₂NH-cyclopropyl.
- 30

19. A compound according to claim 17, wherein R_1 is $-S(=O)_2Me$ or $-S(=O)Me$.
20. A compound according to claim 1, wherein R_1 is $-C(=O)OR_x$, $-C(=O)NR_xR_x$, $-C(=O)NHNH_xR_x$ or $-C(=O)NHCH_2COOR_x$.
21. A compound according to claim 20, wherein R_1 is $-C(=O)OH$, $-C(=O)OMe$, $-C(=O)NH_2$, $-C(=O)NHMe$, $-C(=O)NHNH_2$, $-C(=O)NHCH_2COOH$.
22. A compound according to claim 20, wherein R_1 is $-C(=O)NR_x'-N$ -morpholine, $-C(=O)NR_x'-N$ -piperidine, $-C(=O)NR_x'-N$ -pyrrolidine or $-C(=O)NR_x'-N$ -piperazine, where R_x is methyl, acetyl or preferably H.
23. A compound according to claim 1, wherein R_1 is $-NR_xR_x$, $-N(C=O)C_1-C_4$ -alkyl or $-NHC(=O)CH_2OC_1-C_3$ -alkyl- $COOR_x$.
24. A compound according to claim 23, wherein R_1 is $-NH_2$, $-NHC(=O)Me$ or $NHC(=O)CH_2OCH_2C(=O)OH$.
25. A compound according to claim 1, wherein R_1 is $-C_1-C_3$ -alkyl- $COOR_x$; $-C_1-C_3$ alkyl- OR_x , $-(O-C_1-C_3$ alkyl) $_q$ - $O-R_x$ or a 5 membered ring having 1-3 hetero atoms.
26. A compound according to claim 25, wherein R_1 is carboxyethyl or a methyl ester thereof, 2-methoxyethoxyethoxy or triazolyl.
27. A compound according to claim 1, wherein R_1 is para to the ether linkage.
28. A compound according to claim 1, wherein the ring containing A is phenyl or pyrid-3-yl.
29. A compound according to claim 1, wherein R_2 is hydrogen or fluoro.
30. A compound according to claim 1 where R_2 is meta to the ether linkage.
31. A compound according to claim 1 denoted N-[(1S,1aR,7bR)-4,7-difluoro-1,1a,2,7b-tetrahydrocyclopropa[c]chromen-1-yl]-N'-[5-(4-(sulfonamido)phenoxy)-2-pyridinyl]urea.

32. A pharmaceutical composition comprising a compound as defined in any
5 preceding claim and a pharmaceutically acceptable vehicle or diluent therefor.

33. A composition according to claim 32, further comprising 1 to 3 additional HIV
antivirals.

10 34. A composition according to claim 32, further comprising a cytochrome P450
modulator, such as ritonavir.

35. Use of a compound as defined in any of claims 1-31 in the manufacture of a
medicament for the prophylaxis or treatment of HIV-1 infections.

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36. Use according to claim 35, wherein the HIV-1 infection is a drug escape
mutant.

37. Use according to claim 36, wherein the drug escape mutant comprises the
20 L100I and K103N mutations.